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1: [Ann Surg.](#) 1991 Aug;214(2):155-67.

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Dose response of fish oil versus safflower oil on graft arteriosclerosis in rabbit heterotopic cardiac allografts.

[Yun KL](#), [Fann JI](#), [Sokoloff MH](#), [Fong LG](#), [Sarris GE](#), [Billingham ME](#), [Miller DC](#).

Department of Cardiovascular Surgery, Stanford University School of Medicine, California.

With the advent of cyclosporin A, accelerated coronary arteriosclerosis has become the major impediment to the long-term survival of heart transplant recipients. Due to epidemiologic reports suggesting a salutary effect of fish oil, the dose response of fish oil on graft coronary arteriosclerosis in a rabbit heterotopic cardiac allograft model was assessed using safflower oil as a caloric control. Seven groups of New Zealand White rabbits (n = 10/group) received heterotopic heart transplants from Dutch-Belted donors and were immunosuppressed with low-dose cyclosporin A (7.5 mg/kg/day). Group 1 animals were fed a normal diet and served as control. Group 2, 3, and 4 animals received a daily supplement of low- (0.25 mL/kg/day), medium- (0.75 mL/kg/day), and high- (1.5 mL/kg/day) dose fish oil (116 mg n-3 polyunsaturated fatty acid/mL), respectively. Group 5, 6, and 7 animals were supplemented with equivalent dose of safflower oil (i.e., 0.25, 0.75, and 1.5 mL/kg/day). Oil-supplemented rabbits were pretreated for 3 weeks before transplantation and maintained on the same diet for 6 weeks after operation. The extent of graft coronary arteriosclerosis was quantified using computer-assisted, morphometric planimetry. When the animals were killed, cyclosporin A was associated with elevated plasma total cholesterol and triglyceride levels in the control group. While safflower oil prevented the increase in plasma lipids at all dosages, fish oil ameliorated the cyclosporin-induced increase in total cholesterol only with high doses. Compared to control animals, there was a trend for more graft vessel disease with increasing fish oil dose, as assessed by mean luminal occlusion and intimal thickness. A steeper trend was observed for increasing doses of safflower oil; compared to the high-dose safflower oil group, animals supplemented with low-dose safflower oil had less mean luminal occlusion (16.3% +/- 5.9% versus 41.4% +/- 7.6%, p less than 0.017) and intimal thickness (7.9 +/- 1.9 microns versus 34.0 +/- 13.0 microns, analysis of variance: p = 0.054). Low-dose safflower oil also had a slight, but nonsignificant, beneficial effect on graft vessel disease when compared to control rabbits. The same trends were observed in the degree of histologic rejection (0 = none to 3 = severe) in fish oil- and safflower oil-treated animals. Rejection score correlated weakly but significantly (p = 0.0001) with mean luminal occlusion (r = 0.52) and intimal thickness (r = 0.46). Therefore allograft coronary disease in this model appeared to exhibit an unfavorable, direct-dose response to fish oil and safflower oil, independent of effects on plasma lipids.(ABSTRACT TRUNCATED AT 400 WORDS)

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